

REMARKS

Reconsideration of Finality

Applicants believe that the rejections of Claims 1-5, 8, 15-20 and 37-40 under 35 U.S.C. §§102 and 103, are not necessitated by Applicants' amendment of June 18, 2003. The language that was the subject of the previous Amendment ("at least one informative gene" amended to "two or more informative genes") is irrelevant with respect to the art cited by the Examiner in the Office Action of September 9, 2003. If the Examiner's assertions regarding the teachings of Gocke *et al.*, the reference currently used to reject Claims 1, 3, 4, 8, 15 and 17-19 under 35 U.S.C. §102, were accurate, then the reference would have read on "at least one informative gene" in addition to "two or more informative genes." Therefore, the objection could have been raised in the Office Action of December 18, 2002. Notwithstanding Applicants' belief (detailed below) that the rejections based on Gocke *et al.* should be reconsidered and withdrawn, Applicants nonetheless believe that the Office Action mailed on September 9, 2003 is not properly made final in view of this rejection. Reconsideration of the finality of the Office Action mailed September 9, 2003 is respectfully requested.

Amendments to the Claims

Applicants have canceled Claims 6, 7, 11-14, 21, 22 and 25-36 as drawn to non-elected subject matter. Applicants have amended Claims 1, 3, 4, 15, 18, 19 and 37-40 to more particularly point out and distinctly claim that which Applicants regard as their invention. The scope of the claims has not been narrowed, and no new matter has been added. Entry of the amendments is respectfully requested.

Rejection of Claims 1, 3, 4, 8, 15 and 17-19 Under 35 U.S.C. §102

Claims 1, 3, 4, 8, 15 and 17-19 are rejected under 35 U.S.C. §102 as being anticipated by Gocke *et al.* (U.S. Patent Number 6,156,504, Reference A in the Office Action). The Examiner asserts that Gocke *et al.* teach a method of classifying a lymphoma sample according to predicted treatment outcome comprising the steps of a) isolating a gene expression product from at least two or more informative genes from one or more cells in the sample; and b) determining a gene expression profile of two or more informative genes.

Applicants respectfully disagree. Gocke *et al.* disclose a method for identifying variants, particularly in extracellular DNA. They do not describe a method of isolating a gene expression product and do not disclose a method for determining a gene expression profile.

Applicants describe gene expression products in the Specification as follows: “gene expression products are proteins, peptides, or nucleic acid molecules (*e.g.*, mRNA, tRNA, rRNA, or cRNA) that result from transcription or translation of a gene.” (Page 7, lines 2-5). It is clear that the extracellular DNA assessed by Gocke *et al.* cannot be a gene expression product because it is not the result of transcription or translation of a gene, *i.e.*, it is the DNA that must be transcribed to produce a gene expression product. Furthermore, Gocke *et al.* do not disclose determining a gene expression profile from one or more gene expression products. Although the methods disclosed by Gocke *et al.* may be useful for predicting the likelihood of disease or treatment outcome, these methods are based on genotyping (*e.g.*, the identification of particular alleles in a patient sample) rather than determining a gene expression profile (*e.g.*, the level of one or more gene expression products).

Accordingly, because Gocke *et al.* do not teach or suggest all elements of the claimed invention (*e.g.*, do not teach or suggest gene expression products or gene expression profiles), Gocke *et al.* do not anticipate the claimed invention. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 2 and 16 Under 35 U.S.C. §103(a)

Claims 2 and 16 are rejected under 35 U.S.C. §103(a) as being unpatentable over Gocke *et al.* in view of Dalla-Favera and Chaganti (U.S. Patent Number 5,882,858, Reference AT). In addition to the teachings of Gocke *et al.* (above), the Examiner asserts that the teachings of Dalla-Favera and Chaganti render performing the invention of Claims 2 and 16 obvious, as Dalla-Favera and Chaganti teach an assay for non-Hodgkin’s lymphoma, a method for screening putative therapeutic agents for treatment of non-Hodgkin’s lymphoma and a method for diagnosing B-cell lymphoma. The Examiner asserts that it would have been obvious to one of skill in the art to use the method taught by Gocke *et al.* for diffuse large cell lymphoma in light of the teachings of Dalla-Favera and Chaganti.

Applicants respectfully disagree. As stated above, Gocke *et al.* do not teach the methods of Claims 1 or 15, because Gocke *et al.* do not teach the isolation of gene expression products, nor do they teach determining a gene expression profile based on isolated gene expression products. Dalla-Favera and Chaganti merely describe additional methods for genotyping samples based on isolating genomic DNA, and they do not remedy the defects of Gocke *et al.* Therefore, the teachings of Gocke *et al.* combined with those of Dalla-Favera and Chaganti cannot render Applicants' claimed invention obvious as they do not teach every element of the claimed invention.

In light of Applicants' remarks, reconsideration and withdrawal of the rejection are respectfully requested.

Rejection of Claims 5, 20 and 37-40 Under 35 U.S.C. §103(a)

Claims 5, 20 and 37-40 are rejected under 35 U.S.C. §103(a) as being unpatentable over Gocke *et al.* in view of Perou *et al.* (1999, *Proc. Natl. Acad. Sci. USA*, 96:9212-9217). In addition to the teachings of Gocke *et al.* (above), the Examiner asserts that the teachings of Perou *et al.* render performing the invention of Claims 5, 20 and 37-40 obvious, as Perou *et al.* teach the use of DNA microarrays to demonstrate differences in the pattern of gene expression between normal human mammary epithelial cells and breast cancer.

As stated above, Gocke *et al.* describe methods based on genotyping. Genotyping involves the qualitative identification of a particular allele at a gene locus. Gocke *et al.* do not disclose a method for determining a gene expression profile from one or more gene expression products as discussed more fully above. Although Perou *et al.* describe the use of microarrays, such arrays being useful for quantitatively measuring levels of gene expression products, there is no motivation to combine the references because quantitative analysis is completely irrelevant to the genotyping methods described by Gocke *et al.* One of ordinary skill in the art would not genotype a sample according to the methods of Gocke *et al.* by quantitatively measuring the levels of gene expression products in a sample, because such a quantitative measurement is inappropriate for determining the particular allele present at a gene locus. Therefore, Applicants' claimed invention is not rendered obvious in light of the teachings of Gocke *et al.* combined with

the teachings of Perou *et al.*, because one of skill in the art would not have combined the teachings of the two references.

In light of the above remarks, reconsideration and withdrawal of the rejection are respectfully requested.

CONCLUSION

In view of the above amendments and remarks, it is believed that all claims are in condition for allowance, and it is respectfully requested that the application be passed to issue. If the Examiner feels that a telephone conference would expedite prosecution of this case, the Examiner is invited to call the undersigned.

Respectfully submitted,

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